Preparing Aspirin

**Background:** A component of willow tree bark called salicin has long been recognized as an analgesic (pain reliever) and antipyretic (fever reducer). A powdered derivative of salicin, acetylsalicylic acid, is sold as the common drug, aspirin.

Acetylsalicylic acid (aspirin) is the product of the reaction of acetic anhydride with salicylic acid. The reaction is acid catalyzed by the sulfuric acid ($\text{H}_2\text{SO}_4$ will increase the reaction speed, but does not undergoes itself a chemical change).

If we add the reactants in the molar ratio indicated by the stoichiometry of the reaction and the reaction proceeds to completion, only products will be present at the end. If we add an excess of one of the reactants, the maximum amount of aspirin that we can produce will be determined by the molar amount of the reactant not present in excess. This reactant is called the limiting reactant, because it determines the theoretical product yield. You have an example of calculation for the limiting reactant, theoretical yield and % yield on next page.

**Purpose:** Synthesize aspirin and determine the feasibility of the synthetic methodology using percent yield. The purity of the product is confirmed by measuring its melting point range.

**Safety Considerations:** This experiment uses salicylic acid, acetic anhydride and phosphoric acid (as catalyst). The salicylic acid and aspirin may cause irritation to your skin or eyes, but are basically not hazardous. An excess of these can be disposed of in the sink or if packaged, in the trash. If you spill some, wipe it up with a wet paper towel and throw the towel in the trash. The acetic anhydride and phosphoric acid can cause bad burns. Use them in the hood. Be sure to wear gloves and safety goggles when using these chemicals. Excess chemicals must be disposed of in the plastic tub of water. This will convert the acetic anhydride to vinegar and dilute the phosphoric acid. If you spill a lot of either of these, notify your instructor.

**Equation 1:**

$$\text{HOOC-C}_6\text{H}_4\text{-OH} + \text{CH}_3\text{-COOOC-CH}_3 \rightarrow \text{HOOC-C}_6\text{H}_4\text{-OCOCH}_3 + \text{CH}_3\text{COOH}$$

Salicylic acid       acetic anhydride        acetylsalicylic acid     acetic acid
(aspirin)
Example

**Problem**  Calculate the percent yield if 1.963 g of aspirin is produced from 2.198 g of salicylic acid and 4.0 mL of acetic anhydride.

**Solution**

1. Calculate the number of moles of salicylic acid present in the reaction mixture, using Equation 2.

\[
\text{number of moles of salicylic acid, mol} = \left( \frac{\text{mass of salicylic acid, g}}{13812 \text{ g salicylic acid}} \right) \left( \frac{1 \text{ mol salicylic acid}}{13812 \text{ g salicylic acid}} \right) \quad (\text{Eq. 2})
\]

\[
= \left( \frac{2.198 \text{ g salicylic acid}}{13812 \text{ g}} \right) \left( \frac{1 \text{ mol salicylic acid}}{13812 \text{ g salicylic acid}} \right) = 1.591 \times 10^{-2} \text{ mol}
\]

2. Calculate the mass of acetic anhydride used, using Equation 3. The density of acetic anhydride is 1.082 g/mL.

\[
\text{mass of acetic anhydride, g} = \left( \frac{\text{volume of acetic anhydride, mL}}{\text{density of acetic anhydride, g/mL}} \right) \quad (\text{Eq. 3})
\]

\[
= \left( \frac{4.0 \text{ mL}}{1.082 \text{ g/mL}} \right) = 4.3 \text{ g}
\]

3. Calculate the number of moles of acetic anhydride present in the reaction mixture, using a modification of Equation 2. The molar mass of acetic anhydride is 102.09 g/mol.

\[
\text{number of moles of acetic anhydride, mol} = \left( \frac{4.3 \text{ g acetic anhydride}}{102.09 \text{ g acetic anhydride}} \right) \left( \frac{1 \text{ mol acetic anhydride}}{102.09 \text{ g acetic anhydride}} \right) = 4.2 \times 10^{-2} \text{ mol}
\]

4. Based on the number of moles of each reagent present and the stoichiometry of the reaction, determine the limiting reactant for this preparation. Salicylic acid is the limiting reactant.

5. Calculate the theoretical yield for this preparation, based on the number of moles of limiting reactant present and Equation 4. The molar mass of aspirin is 180.15 g/mol.

\[
\text{theoretical yield, g} = \left( \frac{\text{number of moles of limiting reactant, mol}}{1 \text{ mol aspirin}} \right) \left( \frac{1 \text{ mol aspirin}}{180.15 \text{ g aspirin}} \right) \quad (\text{Eq. 4})
\]

\[
= \left( \frac{1.591 \times 10^{-2} \text{ mol salicylic acid}}{1 \text{ mol aspirin}} \right) \left( \frac{180.15 \text{ g aspirin}}{1 \text{ mol aspirin}} \right) = 2.866 \text{ g}
\]

6. Calculate the percent yield for this preparation, using Equation 5.

\[
\text{percent yield, } \% = \left( \frac{\text{actual yield, g}}{\text{theoretical yield, g}} \right) \times 100\% \quad (\text{Eq. 5})
\]

\[
= \left( \frac{1.963 \text{ g}}{2.866 \text{ g}} \right) \times 100\% = 68.49\%
\]
Procedure:

1. Weigh out 2.0 g of salicylic acid and place in a 125 ml Erlenmeyer flask.
2. Measure out 4.0 ml of acetic anhydride and add this to your flask. Be sure to do this in the hood and wear your goggles. Don't let the acetic anhydride contact your skin and don't get the vapors in your eyes.
3. Carefully add 5 to 10 drops of 85% H₃PO₄ (instead of sulfuric acid), a catalyst, to the flask and swirl to mix everything thoroughly.
4. Still in the hood, heat the mixture for about 10 min. in a beaker of warm water (70-80 °C).
5. After heating, cautiously add 20 drops of distilled water.
6. Next add 20 ml of distilled water and cool in an ice bath. You can do this at your bench. If crystals do not appear, you can scratch the walls of the flask with a stirring rod to induce crystallization.
7. Filter the solid aspirin through a piece of pre-weighed filter paper using a Buchner funnel and the aspirator. Wash the crystals with 2-3 ml of chilled water. The liquid is mostly water and can be washed down the sink. Allow the air to be drawn through the solid and filter paper for 15 minutes. Be sure to record the filter paper weight in your notebook.
8. Place the filter paper with the product in a watch glass and put it in the oven at 100 °C for about 30 min. until dry.
9. Put the dry aspirin and the filter paper onto a piece of weighing paper and weigh again.
10. Measure the melting point range with the "Meltemp" Apparatus (your instructor will demonstrate) and record it in your notebook. Compare your value to the actual melting point range for pure aspirin, 138-140°C.
11. Calculate the weight of your product by subtracting the weight of the filter paper and weighing paper from the total. The theoretical (maximum) yield is 3.9 grams of pure aspirin. What percent of this amount (3.9g) did you actually prepare? This is your percent yield. Record it in your notebook and turn in your product to your instructor.
# Aspirin

## Data and Calculations

| NAME: ___________________________ | DATE: ______________ |
| PARTNER: ________________________ | SECTION: __________ |

| Mass of salicylic acid used | ___________ |
| Volume of acetic anhydride used | ___________ |
| Mass of acetic anhydride used (Density 1.08 g/mL) | ___________ |
| Mass of aspirin obtained | ___________ |
| Theoretical yield of aspirin | ___________ |
| Percentage yield of aspirin | ___________ |
| Melting point of aspirin | ___________ |

Underline those characteristics listed, which would be likely to be present in a good solvent for aspirin:

- organic
- aliphatic
- polar
- hydrogen bonding
- inorganic
- aromatic
- nonpolar
- non-hydrogen bonding
Aspirin
Post-Laboratory Questions

NAME: ___________________________                                DATE: ______________
SECTION: ___________

1. A student performing this experiment added 0.60 mL of acetic anhydride, instead of 6.0 mL. Did this procedural error affect the theoretical yield of her preparation? Briefly explain.

2. After completing the Procedure, a student noticed that, although his aspirin crystals appeared to be dry, the filter paper was still damp. He went ahead and performed the weighing as directed in Step 10, then went on to finish the experiment. Did the damp filter paper affect any of the following? In each case, briefly explain your answer.

(a) Theoretical yield

(b) Calculated actual yield

(c) Calculated percent yield
1. What hazards should you be aware of when working with the following chemicals?

(a) Acetic anhydride

(b) Concentrated sulfuric acid or phosphoric acid (used as catalysts)

2. Explain the following terms as they relate to this experiment.

(a) Acid-catalyzed reaction

(b) Limiting reactant

(c) Analgesic

3. Following the Procedure described in this experiment, a student reacted 2.005 g of salicylic acid with 4.0 mL of acetic anhydride and recovered 1.206 g of aspirin.

(a) Calculate the number of moles of salicylic acid present in the reaction mixture.

(b) Calculate the mass of acetic anhydride used.
(c) Calculate the number of moles of acetic anhydride present in the reaction mixture.

(d) Based on the number of moles of each reactant and the stoichiometry of the reaction, determine the limiting reactant in the preparation.

(e) Calculate the theoretical yield of the preparation, based on the number of moles of limiting reactant present.

(f) Calculate the percent yield of the preparation.